IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327**
THIS DOCUMENT RELATES TO: **WAVE 12 CASES**	**JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

MEMORANDUM OF LAW IN SUPPORT OF MOTION TO EXCLUDE THE OPINIONS AND TESTIMONY OF DR. VLADIMIR IAKOVLEV

Dr. Vladimir Iakovlev is an anatomical pathologist designated as an expert witness by Plaintiffs to offer opinions regarding Ethicon's mesh products. Although the Court has permitted Dr. Iakovlev to testify on some issues in prior cases,[1] a new FDA definition of "degradation," new case law, testing, and scientific literature prove that his methods are unreliable. Moreover, Dr. Iakovlev's opinions have been excluded at least 29 times in mesh litigation, and this Court should do likewise. *See, e.g.*, *Young v. Mentor Worldwide LLC*, 312 F. Supp. 3d 765, 770–72 (E.D. Ark. 2018) (excluded entirely). Pursuant to Federal Rule of Evidence 702 and *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993), Defendants, Ethicon, Inc., and Johnson & Johnson (collectively, "Ethicon"), move to exclude Dr. Iakovlev's opinions as set forth below.[2]

ARGUMENT

I. Legal Standard

Ethicon incorporates by reference the standard of review for Daubert motions as articulated by the Court in *Edwards v. Ethicon, Inc.,* 2014 WL 3361923 (S.D. W. Va. July 8, 2014).

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[1] *E.g.,* Mem. Op. and Order (*Daubert* Motion re: Vladimir Iakovlev, M.D., No. 2:12-md-02327 (S.D. W. Va. Sept. 1, 2016) [ECF # 2710] ("Wave 1 Iakovlev Order").
[2] The cases to which this motion applies are identified in Ex. QQ.

II. The Court Should Exclude Dr. Iakovlev's Degradation Opinions.

Dr. Iakovlev seeks to opine that Prolene mesh degrades in the human body and this can cause adverse clinical effects. Although Dr. Iakovlev admits that one cannot diagnose a medical complication based on the review of mesh pathology specimens, he nonetheless plans to do just that in these cases. His opinions should be excluded.

The theory underlying Dr. Iakovlev's degradation opinions is that the Prolene mesh degrades in the body (*in vivo*) such that cracks on the surface trap histological stains, creating an outer layer visible under light microscopy. Dr. Iakovlev has described this phenomenon as "bark" around the fiber. He opines that this mesh degradation occurs through chemical oxidation. *See* Ex. A, Report 77–94. All of the other degradation opinions Dr. Iakovlev offers depend on this purported observation.[3] As discussed below, Dr. Iakovlev's theory and his underlying methodology are contrary to the FDA's guidance, not generally accepted in the scientific community, have not been subject to valid testing, and are not supported by published scientific literature. *See Daubert*, 509 U.S. at 593 (identifying "whether the theory or technique has been subjected to peer review and publication", "general acceptance" in the relevant scientific community, and whether a theory or technique "can be (and has been) tested" as key indicia to determine the reliability of expert testimony).

[3] Previously, the Court did not credit Ethicon's argument on the grounds that "Dr. Iakovlev's testimony on degradation generally is extensively supported with specific references to the scientific literature and several internal documents." Mem. Op. and Order (Daubert Motion re: Vladimir Iakovlev), at 6 (S.D. W. Va. Sept. 1, 2016) [ECF # 2710]. But Ethicon respectfully submits that, without his bark theory, Dr. Iakovlev's opinion that Prolene degrades in vivo constitutes a materials science opinion that he is not qualified to offer. *See* Ex. E, Bellew 3/5/15 Trial Tr. 696:13-20 (admitting that he is not a materials scientist, and has not consulted with one); Ex. F, Iakovlev 3/18/14 Huskey Dep. 211:15-17 (did not consult a materials scientist). Dr. Iakovlev's alleged detection of histological stain trapped in the degraded surface of Prolene is the only aspect of his degradation opinions related to his knowledge, skill, experience, training, or education as a pathologist. Absent these purported observations, Dr. Iakovlev offers opinions about the condition of the surface of a polymer simply by pointing to studies and internal Ethicon documents that bear no relationship whatsoever to pathology.

A. The FDA Rejects Dr. Iakovlev's Definition of Degradation.

In June of 2016, the FDA issued it's "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process." See Ex. RR. And in this regulatory guidance document the FDA expressly defines "degradation" as follows: "Degradation – decomposition of the device, possibly through the generation of new chemicals or absorption of the material, leading to loss of mechanical and/or physical properties of the device (device function) over time." Id. at 63.

As this Court is aware, Dr. Iakovlev has never tested the mechanical or physical properties of the mesh. Rather, he simply looks at the surface of the mesh, identifies what he says are surface cracks, and calls those surface cracks "degradation." Dr. Iakovlev, by his own admission, has never done any testing to determine whether this putative surface cracking causes the mesh to lose its "mechanical and/or physical properties." Ex. SS at pages 121-123. Because he has conducted no testing to meet the FDA's definition of degradation, Dr. Iakovlev should be barred from testifying about degradation.[4]

B. Dr. Iakovlev's Novel Degradation Theory Is Not Generally Accepted.

Dr. Iakovlev stated he is the first person to propose the theory that degraded Prolene traps stain such that it can be observed via light microscopy. *See* Ex. B, V. Iakovlev, Pathology of Explanted Transvaginal Meshes, 8 Int'l J. of Med., Health, Pharm. and Biomed. Engineering, at 512 (2014) (degradation "bark" "escaped pathologists for over 50 years."); Ex. C, Iakovlev *In re Bos. Sci.* 12/17/2014 Dep. 194:4–6 ("I'm the first one who is describing light microscopy features of

[4] In a recent trial Dr. Iakovlev conceded that he had done no testing to meet the FDA's definition:
Q: "So it's fair to say that you have not – because – well, that you have not tested the device function, meaning the entire device rather than the mesh along, over time, correct?"
A: "That's correct."
Q: "So you would not be able to offer the Court any opinions about whether Ethicon's vaginal mesh products satisfied this definition, correct?"
A: "To this definition in this document, that's correct." Ex. SS at pages 121-123.

polypropylene degradation.").

Dr. Iakovlev admitted his theory is not based on prior studies, *see* Ex. D, Iakovlev 9/11/2015 Dep. 36:10–16 (did not consult anyone for his oxidation testing because "[n]obody ever did it before"), and that there is no published scientific literature describing degradation bark in polypropylene other than his own, *see* Ex. PP, Iakovlev, *Degradation of Polypropylene* In Vivo, at 7 ("[W]e found no description of these findings in published literature after a search through online and printed sources."); Ex. F, Iakovlev 3/18/2014 Dep. 275:8–15. Dr. Iakovlev co-authored a review noting that "the question of whether polypropylene degrades *in vivo* has not been fully resolved, despite decades of use." *See* Ex. G, Blaivas, *Safety Considerations for Synthetic Sling Surgery*, Nature Rev. Urol., at 17 (2015).

Although Dr. Iakovlev has pushed his degradation "bark" theory in pelvic mesh litigation for several years, he fails to identify a single peer-reviewed article—which he also did not co-author—that has adopted his theory. Thus, it cannot be said that Dr. Iakovlev's novel theory has garnered general acceptance by the scientific community. *See, e.g.*, Ex. C, Iakovlev 12/17/2014 *In re Bos. Sci.* Dep. 239:15–240:2 (admitting that his own article is the only published paper reporting that degraded polypropylene traps histological dyes). Accordingly, the "general acceptance" *Daubert* factor requires exclusion of Dr. Iakovlev's degradation "bark" theory.

C. Dr. Iakovlev's Degradation Opinions Are Based on an Untested Hypothesis.

Proper "scientific methodology involves generating hypotheses and testing them to see if they can be falsified." *Nease v. Ford Motor Co.*, 848 F.3d 219, 232 (4th Cir. 2017). Dr. Iakovlev's degradation opinions are inconsistent with the scientific method because they are based on a testable hypothesis that he admits he has not tested.

Dr. Iakovlev concedes his theory is capable of being tested by intentionally oxidizing pristine Prolene to determine (i) whether it degrades and, if so, (ii) whether it holds stain. *See* Ex. D, Iakovlev 9/11/15 Dep. 31:14–46:13 (discussing testing). Dr. Iakovlev testified in September 2015 that he was

conducting such a test to validate his hypothesis. *Id.*[5] In March 2016, Dr. Iakovlev admitted that he had not concluded this test. *See* Ex. J, Iakovlev 3/21/2016 *Stubblefield* Dep. 64:19–65:4. It has been nearly four years since Dr. Iakovlev claimed he was testing his "bark" theory, but he still has not subjected any results to *Daubert* scrutiny.

Moreover, Dr. Iakovlev admitted that he "cannot detect oxidation," the supposed mechanism of *in vivo* degradation of Prolene. Ex. K, Iakovlev 4/3/2019 *Susong* Dep. 150:24-151:5; *see also* Ex. A, Report 77 (discussing oxidation). Thus, the foundational premise on which all of Dr. Iakovlev's degradation opinions rests is merely an untested hypothesis. "[T]he courtroom is not the place for scientific guesswork, even of the inspired sort. Law lags science; it does not lead it." *Rosen v. Ciba-Geigy Corp.*, 78 F.3d 316, 319 (7th Cir. 1996).

D. Ethicon's Experts Have Tested and Disproven Dr. Iakovlev's Hypothesis.

In *Nease v. Ford Motor Co.*, the Fourth Circuit emphasized that, not only had the plaintiff's expert failed to validate his theory with testing, but the defendant's expert (Dr. Steven MacLean) had disproven a component of the plaintiff's expert's hypothesis through testing. 848 F.3d 219, 225 (4th Cir. 2017). The court observed that the plaintiff's expert "never tested [the truck] to determine whether it is actually possible" for his theory to occur. *Id.* at 232. Instead, he "simply relied upon his [visual] observations" of the speed control cable via a fiber-optic tool commonly used by vehicle engineers. *Id.* at 226. The same flaws renders Dr. Iakovlev's testing unreliable.

[5] Even in this incomplete test, Dr. Iakovlev failed to follow the scientific method. He did not prepare or follow a testing protocol, (Ex. D, Iakovlev 9/11/15 Dep. 32:24–33:6); has no lab documentation, (*id.* at 35:2–13); could not identify the meshes being tested, (*id.* at 34:21–35:1), or even the number of samples, (*id.* at 32:9–12); and could not identify the composition of the oxidative medium, (*id.* at 34:5–14). Further, he frequently contradicts himself as to the amount of time necessary for degradation to occur. *Compare* Ex. H, Iakovlev 4/19/2016 *Ramirez* Dep. 394:15–21 (degradation appears at 1 year) *with* Ex. I, Iakovlev 3/4/2016 *Vignos-Ware* Dep. 39:11–24 (degradation observed at 8 months). Dr. Iakovlev's failure to adhere to any protocols or controls renders his opinions unreliable.

To determine the validity of Dr. Iakovlev's theory, Ethicon retained the same expert discussed in *Nease*—Dr. MacLean—who used scientific methods to test Dr. Iakovlev's hypothesis. *See* Ex. L, MacLean Report. To do so, Dr. MacLean intentionally oxidized Prolene mesh samples, then applied the same stains used by Dr. Iakovlev to the samples to determine whether the Prolene retained the stain. *Id.* at 88–98. Specifically, Dr. MacLean intentionally oxidized Prolene mesh samples using two methods: (i) exposure to UV radiation, and (ii) exposure to the oxidative medium used by Drs. Guelcher and Dunn—two materials experts Plaintiffs have designated in the MDL. *Id.* at 88–91. Dr. MacLean's analysis using both approaches proved that even intentionally oxidized Prolene does not trap histological stain. *Id.* at 93–97.

In stark contrast, Dr. Iakovlev did not conduct any tests to validate his bark theory. Rather, like the expert in *Nease*, Dr. Iakovlev simply relied on his visual observations of "bark" to support his degradation opinions. *See* 848 F.3d at 226. By his own admission, Dr. Iakovlev's methods cannot identify whether the "bark" contains oxidized polypropylene. And like the expert in *Nease*, Dr. Iakovlev's unreliable opinions should be excluded.

Thus, Dr. MacLean—using a valid, documented, and repeatable scientific methodology—has established that Dr. Iakovlev's methods are flawed. This is not a case of mere disagreement between the results offered by the parties' experts. Dr. Iakovlev has not presented *results* that have been tested and verified; he has offered only a *hypothesis* that is untested and unsupported by scientific literature (as discussed below). *See Nease*, 848 F.3d at 232; *Claar v. Burlington N. R.R.*, 29 F.3d 499, 502–03 (9th Cir. 1994) ("Coming to a firm conclusion first and then doing research to support it is the antithesis of [the scientific] method."). Conversely, Dr. MacLean, aplying the scientific method to Dr. Iakovlev's hypothesis, proved that Dr. Iakovlev's degradation opinion is the product of flawed methodology.[6]

[6] Dr. MacLean's testing was accepted without revision for publication and presentation in a peer-reviewed conference of the Society of Plastics Engineers. Ex. M, MacLean 4/18/2016 Dep. at 129:22–

E. Dr. Iakovlev's Degradation Theory is Not Supported by Scientific Literature.

Setting aside his unreliable "bark" theory, Dr. Iakovlev has no evidence that Prolene degrades in the human body because the scientific literature does not support his opinions. The Court should exclude his degradation opinions for this reason. *See, e.g.*, *Abarca v. Franklin Cty. Water Dist.*, 761 F. Supp. 2d 1007, 1066 n.60 (E.D. Cal. 2011) ("[A] reliable expert would not ignore contrary data, misstate the findings of others, make sweeping statements without support, and cite papers that do not provide the support asserted.").

1. Dr. Iakovlev relies on papers that do not actually support his opinions.

Although Dr. Iakovlev points to a number of articles in an effort to support his degradation opinions, scrutiny of these materials demonstrates that they simply do not stand for the proposition that Prolene implanted in the pelvic floor degrades. *See* Ex. A, Report 77–78. Citation of inapposite scientific literature does not provide an adequate basis for Dr. Iakovlev's opinions. *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) ("[N]othing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the ipse dixit of the expert."); *see also McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1245–47 (11th Cir. 2005); *accord In re Digitek*, 821 F. Supp. 2d 822, 839 (S.D. W. Va. 2011). For instance:

- **Not Prolene and Speculative.** Dr. Iakovlev cites an article by Costello. Ex. A, Report 77; *see also* Ex. O, C.R. Costello, et al., *Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants from a Single Patient*, 14 Surg. Innov. 168 (2007). That paper analyzed three different hernia mesh explants, finding the Bard mesh degraded, but no such evidence for the Ethicon mesh (Proceed). *Id.* at 172–75. The Ethicon "specimen did not possess any visible surface degradation." *Id.* at 175.

131:18; see also Ex. N, S. Benight, Microscopy of Intentionally Oxidized Polypropylene-Based Mesh Material, SPE ANTEC (2016); Ex. M, MacLean 4/18/2016 Dep. at 130:12–17.

- **Cannot Confirm Either Oxidation or Prolene.** Dr. Iakovlev cites a 2010 article by Clave. *See* Ex. A, Report 77, 81; *see also* Ex. P, A. Clave, et al., *Polypropylene as a Reinforcement in Pelvic Surgery Is Not Inert: Comparative Analysis of 100 Explants*, 21 Int. Urogynecol. J. 261 (2010). But the Clave paper, encompassing 100 meshes from multiple manufacturers, expressly states that while there are "hypotheses concerning the degradation of the PP . . . [n]one of these, particularly direct oxidation, could be confirmed in this study." *Id.* at 266.

- **Not Prolene and Not Pelvic Mesh.** Dr. Iakovlev relies on an article by Wood analyzing non-Prolene hernia meshes. Ex. A, Report 78; *see also* Ex. Q, A.J. Wood, et al., *Materials Characterization and Histological Analysis of Explanted Polypropylene, PTFE, and PET Hernia Meshes from an Individual Patient*, 24 J. Mater. Sci. Mater. Med. 1113 (2013).

- **Exposure to Conditions Not Found in the Pelvic Floor.** Dr. Iakovlev cites an article by Jongebloed. Ex. A, Report 77, 132; *see also* Ex. R, W. Jongebloed & J. Worst, *Degradation of Polypropylene in the Human Eye: A SEM Study*, 64 Documenta Opthamologica 143 (1986). This article is inapposite as it addressed sutures implanted in the human eye. All forms of polypropylene, including Prolene, oxidize when exposed to ultraviolet radiation. Thus, the fact that ocular sutures, which are exposed to ultraviolet radiation, oxidize after implantation in the eye is not germane to the Prolene used in the female pelvic floor.

- **Not Prolene and Exposure to Conditions Not Found in the Pelvic Floor.** The paper by Sternschuss and Ostergard—a paid expert for plaintiffs in pelvic mesh—is a literature review of other papers that do not support the proposition that Prolene pelvic meshes degrade. *See* Ex. S, G. Sternschuss, Donald Ostergard, et al., Post-Implantation Alterations of Polypropylene in the Human, 188 J. of Urology 27, 30–31 (2012). For instance, the Costello, Clave, and Williams papers do not address Prolene. *See supra.* And the Jongebloed and Altman papers cited by Sternschuss are inapposite as they examine only sutures implanted in the eye. *See* Ex. R, Jongebloed & Worst; Ex. T, W.

Jongebloed, et al., *Mechanical and Biochemical Effects of Man-Made Fibers and Metals in the Human Eye, A SEM Study*, 61 Documenta Opthamologica 303 (1986); Ex. U, A. Altman, et al., *The Breakdown of Polypropylene in the Human Eye: Is It Clinically Significant?*, 18 Ann. Opthalmol 182 (1986).

- **Unreliable Methodology.** Dr. Iakovlev cites an article by Mary to support his oxidative degradation opinion. Ex. A, Report 77; *see also* Ex. V, C. Mary, et al., *Comparison of the* In Vivo *Behavior of Polyvinylidene Flouride and Polypropylene Sutures Used in Vascular Surgery*, 44 Am. Soc'y Articial Internal Organs J. 199 (1998). The article's authors did not conduct molecular weight analysis or test the mechanical properties of the sutures.[7] Rather, they concluded Prolene sutures had oxidized based on FTIR test results showing a peak at 1,740^{cm-}, which "has been assigned to carbonyl stretching, and identifies the presence of surface oxidation, because the chemical structure of both pure polymers are devoid of this functional group." *Id.* at 201. But the authors failed to recognize that 1,740^{cm-} is also the wavelength for one of the antioxidants used in Prolene, a fact conceded by materials science experts for plaintiffs in pelvic mesh litigation. *See, e.g.*, Ex. W, Mays 3/2/2016 Dep. 104:24–105:3 (admitting that one of the antioxidants used in Prolene has an FTIR signature of 1,740^{cm-}). Thus, the article failed to confirm that the peak at 1,740^{cm-} was oxidation. In addition, the sample preparation process used in the Mary article introduced error into the SEM results. Specifically, the article explains that after explantation, the sutures designated for SEM analysis were treated with either formalin or gluteraldehyde prior to cleaning. Ex. V, Mary, at 200. The authors ignored the fact that both formalin and gluteraldehyde crosslink with the proteinaceous layer on the fibers to form a hardened shell that can manifest as a cracked layer under SEM. *See* Ex. L, MacLean Report 25–26, 51–52, 98–99 (explaining that fixatives used in sample preparation, such as formalin, bond or crosslink with proteins adhered to the surface of an explant to form a hard and brittle shell around the surface of the explant).

[7] Notably, Dr. Iakovlev has likewise never done any such testing on mesh, including Prolene.

- **Antioxidants Work.**[8] Dr. Iakovlev relies on a 1976 article by Liebert to support his opinions that polypropylene is subject to oxidative degradation. Ex. A, Report 77, 132; *see also* Ex. X, T. Liebert, et al., *Subcutaneous Implants of PP Filaments*, 10 J. Biomed. Mater. Res. 939 (1976). But, as materials science experts for plaintiffs have admitted, Liebert actually found that antioxidants are effective in preventing degradation in polypropylene. *See* Ex. Y, Guelcher 3/25/2014 Dep. 73:9–75:2.

2. Dr. Iakovlev relies on unpublished Ethicon documents regarding Prolene sutures that do not support his opinion.

Dr. Iakovlev also seeks to support his opinion that Prolene degrades *in vivo* by referring to certain unpublished Ethicon documents regarding Prolene sutures. *See* Ex. A, Report 168–79. But these internal documents do not support Dr. Iakovlev's degradation opinions. For example:

- Dr. Iakovlev relies on a 1983 Prolene suture test. Ex. A, Report 167–73. But as polymer chemistry experts for plaintiffs admit, the 1983 suture test examined only one fiber explant. *See, e.g.*, Ex. W, Mays 3/2/2016 Dep. 99:9–100:8. He also could not rule out the possibility that the fiber analyzed in the test was damaged during excision. *Id.* at 100:23–101:4.

- Dr. Iakovlev also relies on a 1987 Prolene suture test. Ex. A, Report 174. However, this test does not support Dr. Iakovlev's opinion that Prolene degrades *in vivo*, because it did not report a change in molecular weight in the sutures, which other experts for plaintiffs have acknowledged is a foundational aspect of oxidative degradation. *See* Ex. W, Mays 3/2/2016 Dep. 79:3–80:12; Ex. Z, Jordi 10/30/2013 Dep. 173:25–174:8. Nor did the test make any findings that the sutures' mechanical properties—such as elongation and tensile strength—diminished.

- Dr. Iakovlev also relies on a seven-year dog study conducted by Ethicon. Ex. A, Report 175–79. But Dr. Iakovlev's reliance on the dog study is misplaced because—as materials science experts

[8] Dr. Iakovlev has provided no scientific evidence that the antioxidants in Prolene mesh do not guard against oxidation of the mesh. As discussed previously, Dr. Iakovlev admitted he cannot identify oxidized polypropylene in the outer layer he identifies as "bark".

for plaintiffs concede—the dog study reported no scientifically significant loss of molecular weight. *See* Ex. W, Mays 3/2/2016 Dep. 151:4–14 (admitting it reported no significant loss of molecular weight and no "molecular weight degradation"). The study also shows the sutures were plasticized *in vivo*, which actually improved the toughness of the sutures. *Id.* at 154:2–13.

Ultimately, Dr. Iakovlev's degradation opinions are unsupported by reliable testing or relevant scientific literature, and cannot be said to be the product of a generally accepted methodology. Accordingly, the Court should exclude his degradation opinions at trial.

III. Dr. Iakovlev's Opinions Regarding Clinical Complications Are Unreliable.

A. Dr. Iakovlev Lacks Specialized Knowledge Sufficient to Testify About Potential Injuries to the Female Body.

Dr. Iakovlev intends to opine that alleged defects in the Prolene mesh cause complications in patients. Although Dr. Iakovlev is a medical doctor, the Court should not permit him to testify that Prolene mesh causes complications in areas of the body about which he has no specialized knowledge. Dr. Iakovlev is not a urogynecologist and has no urogynecological training. *See, e.g.*, Ex. I, Iakovlev 3/4/2016 Vignos-Ware Dep. 95:15–19. He has never treated any patient for pelvic organ prolapse, incontinence, mesh complications, or any other medical condition. *See, e.g.*, Ex. AA, Iakovlev 8/12/2014 Dep. 148:25 ("I am not a treating physician."). Moreover, other than reviewing specimens removed and sent to him by other physicians, Dr. Iakovlev does not treat patients. His training and experience in pathology do not qualify him to opine about complications in this case. *See Hines v. Wyeth*, No. 2:04-cv-0690, 2011 WL 2680842, at *7 (S.D. W. Va. July 8, 2011) (expert opinion must not go "beyond the expert[']s qualifications").

B. Dr. Iakovlev's Opinion that Degradation Causes Clinical Complications is Unreliable, Not Generally Accepted, and Contradicts his Own Publications.

Dr. Iakovlev plans to tie his unreliable degradation hypothethesis to his speculative conclusions on clinical complications and testify it is proven that Prolene degradation causes various complications. Ex. A, Report 77–78. Dr. Iakovlev fails to identify any testing or scientific literature

supporting his clinical complications proposition. *See id.* Dr. Iakovlev should be precluded from offering any such opinions on this basis alone.

Moreover, Dr. Iakovlev's publications do not provide a sufficient foundation for him to opine to a reasonable degree of medical certainty that degradation actually causes complications in patients. Indeed, Dr. Iakovlev's publications outside of litigation state only that degradation "*may* play a role" in the development of complications, (Ex. B, V. Iakovlev, *Pathology of Explanted Transvaginal Meshes*, at 512 (emphasis added)), and that studies are necessary to determine if degradation plays a role in causing complications.[9] Simply put: a paper that states "A *may* cause B," is not a legitimate—much less generally accepted—scientific basis for concluding that "A *does* cause B."

The Court should not permit Dr. Iakovlev to testify that degradation of Prolene causes complications when he failed to identify any support for his opinion, and his publications show that no such causal connection has been made, and even cast doubt on whether degradation occurs *in vivo*. *See Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999) (an expert must "employ[] in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field").

[9] *See* Ex. MM, V. Iakovlev, *In Vivo Degradation of Surgical Polypropylene Meshes: A Finding Overlooked For Decades*, 465 Virchows (2014), at 35 ("discovery" of degradation using stains and microscopy "opens the door to study the role of degradation in the development of complications."); Ex. OO, V. Iakovlev, *Explanted Surgical Meshes: What Pathologists and Industry Failed to Do for 50 Years*, 465 Virchows 337 (2014) ("The newly described findings need to be studied in correlation with clinical symptoms to guide future developments."); Ex. B, V. Iakovlev, *Pathology of Explanted Transvaginal Meshes*, at 512 ("Polypropylene degradation *may play a role* in the continuous inflammatory response, mesh hardening, and late deformations" and the "chemical products of degradation *need to be studied* for their composition and effect on the tissue."); Ex. PP, Iakovlev, *Degradation of Polypropylene* In Vivo, at 10 ("[The] exact mechanisms of these late complications are yet to be understood"); Ex. G, Blaivas, at 17 ("the question of whether polypropylene degrades *in vivo* has not been fully resolved, despite decades of use.").

C. Contrary to Generally Accepted Methodology, Dr. Iakovlev Failed to Use a Control in His Histological Analysis.

This Court has previously precluded Dr. Iakovlev from offering "complications opinions based on his examination of explanted mesh samples without the use of a control sample." *In re: Ethicon, Inc. Pelvic Repair Sys. Prod. Liab. Litig.*, No. 2:12-md-02327, 2016 WL 4582228, at *4 (S.D. W. Va. Sept. 1, 2016). The Court reasoned that "[w]ithout a proper control, Dr. Iakovlev's opinions correlating specific complications with samples of explanted mesh products do not provide a sufficiently reliable methodology." *Id.* The same result should obtain here.

Dr. Iakovlev's opinions that Ethicon mesh products cause complications in women are based on his histological analysis of explanted meshes. Dr. Iakovlev's opinions are inconsistent with the scientific method because he failed to compare his histological observations in explanted pelvic meshes to the histology of patients who were symptom-free. *See, e.g.*, *Sanchez v. Bos. Sci. Corp.*, No. 2:12-cv-05762, 2014 WL 4851989, at *28 (S.D. W. Va. Oct. 17, 2014) ("Vigorous adherence to protocols and controls are the hallmarks of 'good science.'").

Dr. Iakovlev's failure to use a control means he cannot eliminate the likelihood that the histological presentation of women suffering from pain is the same as the histology of women not suffering from pain. This is a significant gap in Dr. Iakovlev's analysis because if the histology of both groups is the same, his histological findings cannot identify the cause of the pain.[10]

[10] Although Dr. Iakovlev's report discusses the general use of controls in pathology, he does not discuss the use of a symptom-free control for determining whether alleged clinical complications were caused by a mesh implant or other medical device. *See* Ex. A, Report 17–19. Instead, Dr. Iakovlev only addresses the use of controls (or lack of controls) in diagnosing cancer or heart problems or research involving placebos. *See id.* at 19. This discussion fails to address the fundamental methodological flaw in Dr. Iakovlev's opinions about mesh-related complications: without an asymptomatic comparator, Dr. Iakovlev has no way of distinguishing the histological presentation of a mesh implant that is causing pain (or other complication) from the histological presentation of a mesh implant from a patient who did not experience any mesh-related complications. *See In re: Ethicon, Inc. Pelvic Repair Sys. Prod. Liab. Litig.*, No. 2:12-md-02327, 2016 WL 4582228, at *4 (S.D. W. Va. Sept. 1, 2016) (excluding Dr. Iakovlev's complications opinions because "Dr. Iakovlev did not compare

The same holds true with respect to all of the complications about which Dr. Iakovlev opines. Without a proper control, Dr. Iakovlev's attempt to correlate specific complications with explants is pure conjecture. The Court should preclude Dr. Iakovlev from offering opinions regarding complications on this basis. *See, e.g.*, *McClain v. Metabolife Int'l, Inc.*, 401 F.3d at 1237 ("*Daubert* requires the trial court to act as a gatekeeper to insure that *speculative* and unreliable opinions do not reach the jury." (emphasis added)).

D. Dr. Iakovlev Failed to Account for Relevant Scientific Literature.

Dr. Iakovlev's methodology is unreliable because he failed to account for readily available, contrary scientific literature relevant to his opinions.[11] Courts routinely exclude an expert's opinion "if the relevant scientific literature contains evidence tending to refute the expert's theory and the expert does not acknowledge or account for that evidence[.]" *In re Rezulin Prods. Liab. Litig.*, 369 F. Supp. 2d 398, 425 (S.D.N.Y. 2005); *see also id.* at 425 n.164 (noting courts have excluded expert testimony for failing to account for contrary evidence); *Yates v. Ford Motor Co.*, 113 F. Supp. 3d 841, 858-59 (E.D.N.C. 2015) (same regarding scientific literature); *In re Zoloft Prods. Liab. Litig.*, 26 F. Supp. 3d 449, 459-60 (E.D. Pa. 2014) (excluding expert who failed to distinguish studies directly relevant to her opinions).

Most significantly, Dr. Iakovlev opines that the inflammatory reaction to mesh and the resulting fibrosis can cause pain. *See, e.g.*, Ex. A, Report 20-21, 107, 110. However, in reaching his opinions Dr. Iakovlev did not even consider Dr. Hill's *Histopathology of Excised Midurethral Sling Mesh*, 26 Int'l Urogyncology J. 591 (2015), which directly refutes Dr. Iakovlev's theory. Indeed, Dr. Iakovlev was made aware of the Hill study at a deposition back in 2015 and nearly four years later has offered

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examined tissue slides of patients complaining of pain to slides of tissue from patients who did not complain of pain yet nonetheless had their mesh devices removed").

[11] The Court disagreed with Ethicon's argument on the grounds that "Dr. Iakovlev's alleged failure to review a particular study in forming his opinion is better suited for cross examination[.]" *Id.* at 9. Ethicon respectfully submits, however, that Dr. Iakovlev failed to account for numerous studies directly relevant to his opinions.

no meaningful assessment of this contrary study. *See* Ex. D, Iakovlev 9/11/15 Dep. 152:14–153:8. The Hill study conducted the analysis that Dr. Iakovlev has never done—*i.e.,* using a control and comparing the histological reaction of symptomatic and asymptomatic pelvic meshes. The authors examined 130 explanted meshes, and conducted a histological comparison of the patients who complained of pain and those who did not. Ex. BB, Hill at 592. Contrary to their own hypothesis, they found that pain was *not* associated with increased inflammation. *Id.* at 592-93. They also found no difference in fibrosis between the two groups. *Id.* at 593. Another research group has recently published similar findings. *See* Ex. CC, Li L, Wang X, Park JY, et al. *Pathological findings in explanted vaginal mesh*. Human Pathology 2017; 69: 46-54. Like his treatment of the Hill study, Dr. Iakovlev has neither acknowledged nor addressed this additional literature.

Dr. Iakovlev's failure to account for literature directly relevant to his opinions is not an isolated incident, rendering his opinions unreliable. *In re Rezulin,* 369 F. Supp. 2d at 425.

E. Dr. Iakovlev's own paper proves his methodology is not scientifically legitimate.

In reaching his unqualified and unreliable opinions on clinical complications, Dr. Iakovlev does not "employ[] in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Kumho*, 526 U.S. at 152. A review paper co-authored by Dr. Iakovlev confirms that—outside of the context of litigation—he understands that his approach is speculative. Specifically, the paper states that "[s]everal studies have confirmed" that "when microscopy [is] performed, results of the microscopic examinations usually d[o] not explain the specific complications experienced by the patients." *See* Ex. G, Blaivas, at 15. The paper further explains that "we have an incomplete understanding of interactions specific to a mesh material and design as well as the pathophysiology of any complications." *Id.*[12]

[12] Although this Court has disagreed with the significance of Dr. Iakovlev's concession, Ethicon respectfully submits that an expert should not be permitted to opine about complications based on

Although his own paper reviewed by his peers stated the review of histology is insufficient for correlating complications to mesh, Dr. Iakovlev seeks to do just that for a lay jury. At deposition, however, Dr. Iakovlev has admitted that he could not draw causal conclusions based on his review of histological slides; instead, he "can only estimate the probability." Ex. D, Iakovlev 9/11/15 Dep. 140:14–141:8; *see also id.* at 159:2–160:4 (acknowledging that he could not rule out that "deformed" nerve did not cause pain because "there are many, many, many factors which cause" symptoms); *id.* at 208:25–209:22 (admitting that he cannot opine that mesh caused symptoms in a specific slide because "[c]linical symptoms is [sic] a multifactorial, complex phenomena" but "probability that it will compress urethra is higher"); *id.* at 224:9–225:3 (claiming mesh fibers "[p]robably" irritated the nerve in the slide, but refusing to say the mesh "actually caused symptoms"). The Court should exclude Dr. Iakovlev's opinions because his own writings show that his methodology in this case is insufficient to support conclusions as to the cause of a patient's complications and he conceded at deposition that his efforts to do so are speculative.

IV. Dr. Iakovlev's Opinion that the Presence of an Erosion Necessarily Implies that the Patient had a Wound Infection is Unreliable.

Dr. Iakovlev seeks to opine that Prolene mesh causes erosions in patients, and that the existence of an erosion establishes the presence of a wound infection. *See, e.g.*, Ex A, Report 62-63, 113. Indeed, Dr. Iakovlev testified that "erosion is always associated with localized infection." Ex. DD, Iakovlev 3/13/2016 *McBrayer* Dep. 14:2–6; *see also* Ex. EE, Iakovlev 3/4/2016 *Funderburke* Dep. 25:12 (same); *id.* at 24:17–25:21 (explaining that a "diagnosis was made [of] vaginal erosion, which comes together with infection"). Dr. Iakovlev's infection opinion is simply *ipse dixit*.

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microscopy when his own writings explain that such analysis "d[oes] not explain the specific complications experienced by the patients." *Id.* at 15; *see also* Kumho, 526 U.S. at 152 (expert must "employ the same level of rigor inside and outside of the courtroom).

This Court should again exclude Dr. Iakovlev's infection opinion as "simply not supported with cited scientific literature." *In re Ethicon*, 2016 WL 4582228, at *5. Moreover, Dr. Iakovlev made no effort to adhere to diagnostic criteria in forming his infection opinions. Dr. Iakovlev believes that no such analysis is necessary, because "it's a given that there is infection" any time there is an erosion. *See, e.g.*, Ex. EE, Iakovlev 3/4/2016 *Funderburke* Dep. 24:17–25:21. But it is well-understood in the medical community that certain criteria must be satisfied before an infection can be diagnosed. *See, e.g.*, Ex. FF, Guideline for Prevention of Surgical Site Infection, at 252 (1999) ("SSI Guidelines"). Indeed, the Centers for Disease Control and Prevention publishes criteria for determining whether an infection exists in various circumstances. For example, to diagnose a soft-tissue infection, a patient must have

> (i) organisms identified from tissue or drainage from affected site by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment;
> (ii) purulent drainage at affected site; [or]
> (iii) an abscess or other evidence of infection on gross anatomic or histopathological exam.

Ex. GG, CDC/NHSN Surveillance Definitions for Specific Types of Infections, at 17–25 (Jan. 2016).[13]

V. Dr. Iakovlev's Mesh Folding and Deformation Opinions Are Unreliable.

Dr. Iakovlev opines that mesh can fold or curl *in vivo*; that such deformations can form "compartments"; and that mesh folding, curling, and compartments can cause nerve entrapment. Ex.

[13] A post-operative surgical site infection must involve at least one of the following: Purulent drainage from the deep incision . . . [;] A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following. signs or symptoms: fever (>38°C), localized pain, or tenderness, unless site is culture- negative[;] An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathological or radiologic examination[; or,] Diagnosis of a deep incisional SSI by a surgeon or attending physician. Ex. FF, SSI Guidelines, at 252; see also Ex. JJ, Global Guidelines for the Prevention of Surgical Site Infection, at 38 (2017) (identifying various infection criteria).

A, Report 69–76. This Court should continue to exclude Dr. Iakovlev's opinions on this topic. *See, e.g.*, *In re Ethicon*, 2016 WL 4582228, at *4.

Dr. Iakovlev's claim that he can look at a pathology slide and infer that mesh curled or deformed *in vivo* prior to explantation is unfounded. Dr. Iakovlev failed to follow the standard methodology used by pathologists for determining how a specimen is oriented in the human body. *See* Ex. HH, William Westra, Surgical Pathology Dissection (2003), at 4; Ex. II, Susan Lester, Manual of Surgical Pathology (2010) at 7.[14] Rather, he simply concludes that a specimen that has a "folded" appearance during his examination was also folded *in vivo*. This is rank speculation, and inconsistent with the generally accepted methodology for determining how specimens appeared in the body. Furthermore, Dr. Iakovlev admitted that he is unable to determine whether any alleged deformation occurs during the implantation procedure or *in vivo*. *See, e.g.,* Ex. D, Iakovlev 9/11/15 Dep. 213:12–24, 215:5–13, 216:20–24. Dr. Iakovlev's opinions regarding mesh curling or deformation are speculative and should be excluded.

VI. Dr. Iakovlev Should Not Be Permitted to Offer Opinions Based On Mesh Not At Issue In This Case Or Mesh That He Cannot Identify.

Dr. Iakovlev also seeks to base his opinions in this case on his review of "over 500 specimens of meshes explanted from the female pelvis, from the groin and the anterior abdominal wall." Ex. A, Report 9. But Dr. Iakovlev has previously admitted that many of the meshes in his data pool are not even made of polypropylene, much less Prolene. *See, e.g.,* Ex. KK, Iakovlev *Bellew v. Ethicon* Report 2 (data pool consists of "explanted mesh types includ[ing] . . . knitted polypropylene, GoreTex and combined designs"). Moreover, many of the meshes in his data pool were supplied by plaintiffs'

[14] To ascertain how a specimen was oriented *in vivo*, a pathologist must identify anatomical landmarks and consult markers provided by the surgeon. Specifically, the surgeon must use sutures, tags, or a diagram to designate the orientation (i.e., anterior, posterior, medial, lateral, superior, and inferior positioning) of the specimen. The failure to adhere to this methodology at the time of explantation eliminates the pathologist's ability to determine the *in vivo* orientation of a specimen and renders conclusions as to its *in vivo* appearance speculative. *See* Ex. HH, Westra, at 4; Ex. II, Lester, at 7.

attorneys. *See* Ex. AA, Iakovlev 8/12/2014 Dep. 59:25–60:15.

Similarly, Dr. Iakovlev seeks to explain his opinions using photographs of slides of mesh explants from various sources, many of which he has recycled from prior cases. *See* Ex. A, Report 22–25, 39–41, 43, 52–60, 63–68, 71–76, 83–94, 101–02, 114–16, 118–20, 191. Yet, Dr. Iakovlev has testified that he could not determine the origins of many of his slides. Ex. D, Iakovlev 9/11/15 Dep. 107:15–109:5; *see also id.* at 20:22–21:22 (explaining that he may have received some of his slides from Dr. Kreutzer, who received them from plaintiffs' attorneys). Dr. Iakovlev has also testified that he does not know how many photographs of histology slides in his report depict Ethicon mesh and that the photographs could be from any manufacturer's mesh. *See* Ex. LL, Iakovlev 9/7/18 Dep. 215:11-18, 216:23-217:8, 223:14-22, 226:18-20.

Dr. Iakovlev's opinions based on meshes that are not at issue in this litigation—and that may not even be from an Ethicon product—constitute the same sort of unreliable, irrelevant testimony repeatedly excluded by this Court and others. *See In re Ethicon*, 2016 WL 4582228, at *5 ("Such indeterminacy raises concerns about the integrity of Dr. Iakovlev's data pool, as the selection and origin of samples may necessarily affect the conclusions that may reliably be drawn from them."); *Young*, 312 F. Supp. 3d at 770–72. The same result should obtain here.

VII. Dr. Iakovlev Is Not Qualified to Offer Opinions on the Warnings for Ethicon's Mesh Products.

Dr. Iakovlev's report contains an "analysis" of the instructions for use for various Ethicon mesh products. *See* Ex. A, Report 229–37. Dr. Iakovlev claims that certain risks were "missing" from the IFUs, or that the IFUs are misleading. *See id.* These opinions go beyond Dr. Iakovlev's qualifications as a pathologist and into the realm of legal and regulatory opinions concerning medical device manufacturers' duties to warn.

Dr. Iakovlev is not an expert on designing product warnings, and he has no specialized knowledge concerning the specific information that must be included in the warnings for a medical device. *See*, *e.g.*, *Frankum v. Bos. Sci. Corp.*, No. 2:12-cv-00904, 2015 WL 1976952, at *29 (S.D. W. Va. May 1, 2015). As discussed above, Dr. Iakovlev is not a specialist in treating female pelvic floor conditions and cannot base his warnings opinions from his own experience treating patients – because he does not treat them. Accordingly, his opinions concerning the IFUs for Ethicon's mesh products are beyond his qualifications and should be excluded.

CONCLUSION

For the reasons set forth above, Defendants respectfully request that this Court grant this Motion and enter an Order excluding the opinions and testimony of Dr. Vladimir Iakovlev. Defendants further request that this Court award any other relief it deems just and proper.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on November 4, 2019, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system which will send notification of such filing to CM/ECF participants registered to receive service in this MDL.

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